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# Potentia Poises for Validation in Complement Inhibition in AMD

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With Phase I data expected next month, Potentia Pharmaceuticals Inc. hopes to validate complement inhibition as an approach to treating age-related macular degeneration (AMD).

Multiple papers published in the last few years have established a genetic link between AMD and various complement factors, members of a protein family involved in inflammation and innate immunity. The research sparked a flurry of interest in the field: Potentia President and CEO Cedric Francois said "virtually every large pharma" is looking at complement for AMD.

Preclinical work also is under way with Taligen Therapeutics Inc.'s inhibitors of complement factors B and H, Optherion Inc.'s recombinant complement factor H drug, Ophthotech Corp.'s aptamer targeting complement C5, and Alexion Pharmaceuticals Inc.'s terminal complement blocker eculizumab, which is approved for a blood disorder.

Yet Potentia is unique in its targeting of complement C3, which Francois called the "hub" of all complement activation. Francois said Potentia's broad approach makes sense because seven complement components have been linked to AMD, and it is "too early to be specific."

He noted that specificity for a VEGF subtype crippled wet AMD drug Macugen (pegaptanib sodium, OSI Pharmaceuticals Inc.) against the broader VEGF inhibition offered by its competitor Lucentis (ranibizumab, Genentech Inc.).

Potentia's C3 inhibitor, POT-4, is an optimized version of the small-molecule compstatin designed for administration every three to six months via intravitreal injection. The compstatin family of compounds was discovered at the University of Pennsylvania by John Lambris – whom Francois called the "complement godfather" – and Potentia holds exclusive worldwide rights to the compound class in all fields of use.

Potentia's other differentiating factor, Francois said, is its position at the front of the pack testing complement inhibitors for AMD. The company said its Phase I trial, started in March 2007, was the first to advance the approach into humans.

Data will be presented at the American Academy of Ophthalmology's annual meeting on Nov. 7 by the University of Miami's Philip Rosenfeld – the same ophthalmologist who presented the data supporting the off-label use of Lucentis's less expensive cousin Avastin (bevacizumab) in wet AMD.

The many competitors nipping at Potentia's heels will be watching that presentation closely – as will others in the industry. Francois explained that there are no good animal models for AMD, so those data may be the first to validate a target that was identified solely through the use of genetic data.

But while Potentia couldn't do preclinical pharmacology work without a model, Francois said the company has done extensive preclinical toxicology studies.

He noted that in studies of 196 nonhuman primates, there were no cases of eye infection, a concern that had been raised due to the role of complement in immunity.

If the Phase I data are good, Potentia plans to begin a Phase II trial next year in advanced dry AMD. A separate trial is planned for wet AMD.

Overall, AMD affects more than 50 million people worldwide. An estimated 15 million have wet AMD, a market currently dominated by Lucentis, which generated $815 million in 2007. Late-stage competitors include Regeneron Pharmaceuticals Inc.'s VEGF Trap-Eye and Opko Health Inc.'s bevasiranib, and others at various stages also are seeking to either work with Lucentis or improve on its administration, which requires monthly injections into the eye.

Companies also are looking for ways to stop the progress of AMD.

Francois noted that Lucentis is "very good at stopping the bleeding in the back of the eye but cannot stop the disease process."

He added that the industry is eager to find out if complement inhibition may hold the answer.

There are no drugs approved for dry AMD, although Pipex Pharmaceuticals Inc., Sirion Therapeutics Inc., Othera Pharmaceuticals Inc., Pfizer Inc., Acucela Inc., Ophthotech

and others have programs under way.

Francois estimated that about 1.3 million patients have advanced dry AMD, in which the retina starts to die. He added that doctors are starting to see cases of advanced dry AMD in patients previously treated with Lucentis for wet AMD.

Louisville, Ky.-based Potentia was founded as a nanotechnology company in 2001 but reinvented itself in 2003 with the goal of focusing on AMD. It picked up the rights to compstatin in 2006, raised $5 million in a Series A round in 2007, and raised another $12 million in a Series B round in 2008.

Investors include HealthCare Ventures and MASA Life Science Ventures.

Potentia also raised $2 million through grants and about $4 million in additional funding from angel investors. ■